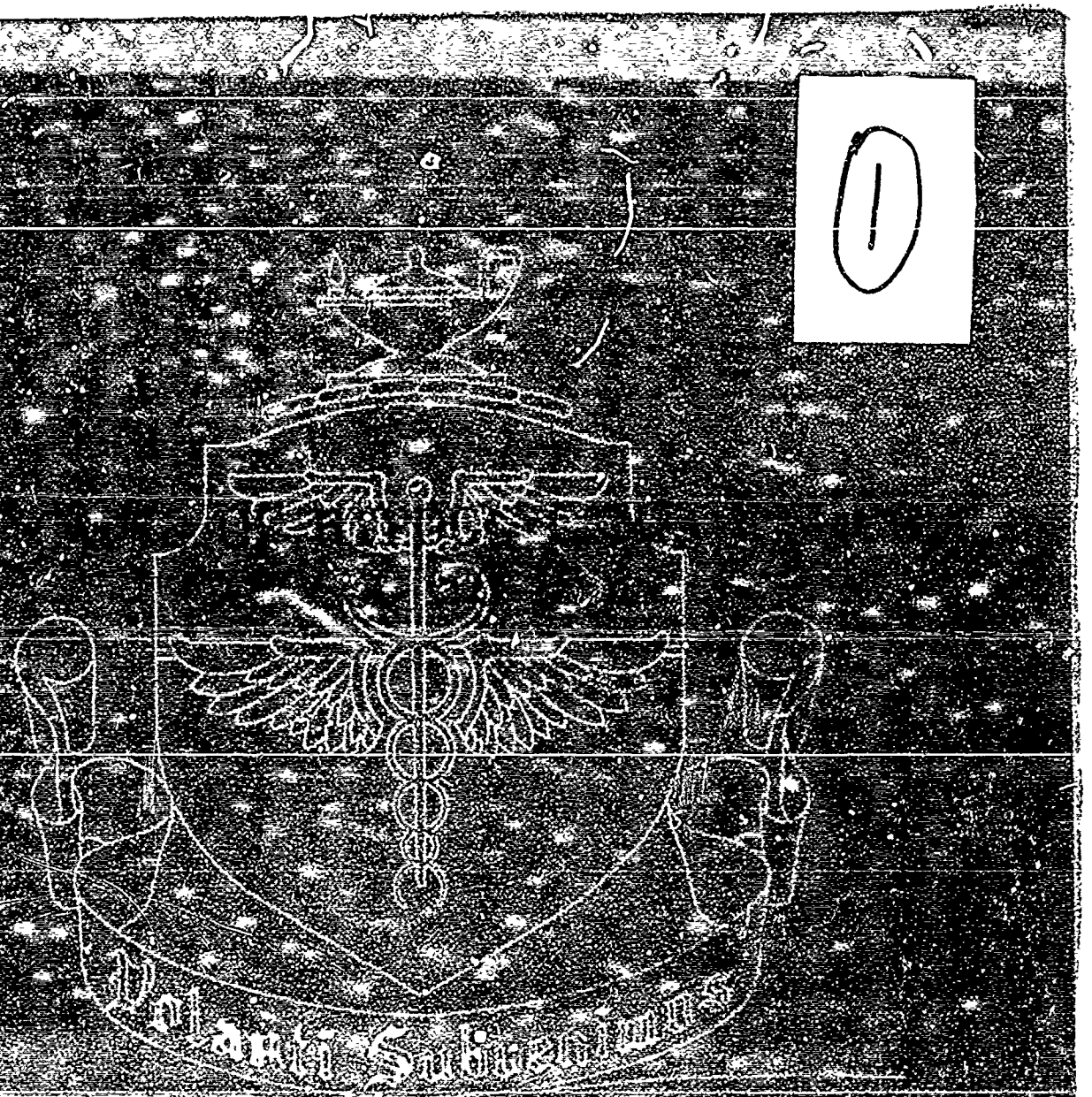
THE CAUSE OF HYPOGLYCEMIA IN DOGS EXPOSED TO HEAT

SCHOOL OF AVIATION MEDICINE
RANDOLPH AIR FORCE BASE, TEXAS

JUNE 1959



THE CAUSE OF HYPOGLYCEMIA IN DOGS EXPOSED TO HEAT

G. S. KANTER, Ph.D.

Department of Physiology
Albany Medical College
Albany, New York

59-38

Air University
SCHOOL OF AVIATION MEDICINE, USAF
RANDOLPH AFB, TEXAS

June 1959

7758-49

THE CAUSE OF HYPOGLYCEMIA IN DOGS EXPOSED TO HEAT

When unanesthetized dogs are exposed to heat, hypoglycemia results. One would expect that the dehydration which also occurs should cause an increase in blood glucose concentration, as is usually found in man. The tendency is present in dogs, but the utilization of glucose is sufficiently rapid to offset the hemoconcentration and cause a fall in glucose levels even when exogenous glucose (11 percent) is given by stomach tube at the rate of 1 percent body wt./hr. This increased utilization has been demonstrated to be due mainly to involvement of the respiratory muscles used in the panting mechanism, since blood glucose does not fall under similar conditions when the animal is curarized. The evidence shows that the hypoglycemic mechanism present in dogs is not a species phenomenon but is probably also present in man under appropriate conditions. In both man and the dog, the occurrence of hypoglycemia depends on the degree of involvement of the respiratory apparatus.

In a previous study (1) we found that when unanesthetized dogs were exposed to high environmental temperatures and low humidity, and were deprived of water, they became dehydrated and, at the same time, hypoglycemic. This finding of a fall in blood glucose concentration in dogs is opposite to that in man (2, 3) under similar environmental conditions. In this study we decided to probe further into the mechanism of regulation of blood glucose in dogs exposed to heat. Why does the blood glucose fall in dogs while it becomes more concentrated in man also subject to heat, dehydration, and consequent hemoconcentration?

METHODS

Thirty-seven experiments were conducted on 12 unanesthetized dogs trained to stand upright, loosely restrained, in a dog stall which was placed on a movable table. The air temperature in the hot room varied from 135° to 105° F. in different experiments and the humidity was maintained below 20 percent. All control periods were run outside the hot room. Body weight of the dogs was measured periodically with a Fairbanks balance accurate to 0.01 kg. The balance was arranged to fit under the dog stall so that it was possible to weigh the animals as desired without disturbing them. Blood samples were taken periodically from the leg veins. Both whole blood and plasma were analyzed for glucose concentration by a modification of the Somogyi technic (4, 5). Plasma phosphate was determined by the Gomori method (6) and pH was determined anaerobically with a Model G Beckman pH meter.

Seven series of experiments were conducted. The first series involved water-loading and was designed to show whether the hydration level of the animals was a factor in the hypoglycemia. In the second series we investigated the handling of exogenous glucose loads by the dogs. The third series was an investigation of the effect of acidosis and alkalosis on glucose regulation. In the fourth series, to test whether or not hypoglycemia could be attributed to an insulinlike action, 1 dog was given sufficient alloxan to destroy the islet cells of the pancreas, after which it was exposed to heat. The possibility that the hypoglycemia was due to acceleration of metabolism was investigated by studying the effect of a lower air temperature (105° F.) on glucose regulation, in the fifth series. The next group, sixth in the series, was tested at a very high temperature (135° F.) to see if glucose regulation would be significantly different from the results obtained at 120° F. Lastly, flaxedil® was given to 2 dogs exposed to heat to study the effect of depressing skeletal muscle activity on glucose regulation.

RESULTS

Effect of hydration level on glucose regulation

Dehydration is a direct factor in concentration of blood constituents; yet it was found

Received for publication on 12 October 1944.

that, concomitant with severe dehydration and hyperthermia, a specific blood constituent (namely, glucose) fell in concentration. Two explanations were initially considered: the hypoglycemia might be a resultant of hyperthermia or it might, in some way, be due to dehydration. That the fall in blood glucose concentration was due to dehydration per se seemed unlikely, but a series of 11 experiments were run to test the effect of varying the hydration level on glucose regulation during exposure to heat. The results showed that in spite of maintenance of hydration by loading water by stomach tube at the rate of 1.5 to 3 percent body wt./hr., or prevention of extensive dehydration by lower rates of loading, glucose levels still fell. The tendency toward hypoglycemia under these conditions, however, was less than that during dehydration. As hypoglycemia occurs whether hydration is maintained or not, it does not appear likely that dehydration is a major factor in the fall of blood sugar, but rather that the hypoglycemia is more directly related to temperature regulation in the face of exposure to heat and hyperthermia.

Regulation of exogenous glucose during exposure to heat

The consistent fall in blood sugar concentration in dogs during exposure to heat and low humidity prompted an investigation of the handling of exogenous loads of glucose under the same conditions. By giving extra glucose, could we prevent the fall in blood sugar? To test this, three different glucose solutions were tried. The first 2 dogs were given 5.5 percent glucose by stomach tube (dosage, 1 percent of body weight) every hour for 4 hours in the hot room. The results in table I show

TABLE I

Handling of glucose loads during exposure to heat

Exper. No.	Air temp. (° F.)	Glucose solution		Whole blood glucose (mg. percent)			Weight (kg.)			Rectal temperature (° F.)		
		Concentration (percent)	Dose (percent body wt./hr.)	Hours			Hours			Hours		
				0	2	4	0	2	4	0	2	4
119	120	5.5	1.0	80.0	93.5	77.8	13.82	13.78	13.64	101.6	103.0	103.3
120		5.5	1.0	102.0	92.0	92.0	18.73	18.36	18.06	102.0	103.9	105.0
121	120	11.0	1.0	86.3	84.4	70.4	14.60	14.45	14.14	101.1	103.1	104.3
122		11.0	1.0	80.0	87.5	66.9	12.28	12.21	12.02	102.1	103.5	104.4
123		11.0	1.0	89.0	89.0	76.0	14.47	14.28	13.96	101.8	103.9	104.6
124	120	5.5	2.0	90.5	77.5	62.0	14.85	14.97	14.94	101.4	102.9	103.5
125		5.5	2.0	74.5	62.0	70.0	11.92	12.16	12.24	103.2	103.7	104.2
126		5.5	2.0	91.7	83.7	68.4	19.68	19.41	19.04	102.3	103.8	104.2
134A	72	11.0	1.0	89.6	106.9	86.8	14.68	14.79	14.75	100.6	100.9	100.8

Results of 9 experiments. Dogs were given glucose solutions by stomach tube every hour for 4 hours, starting just before they entered the hot room. Glucose determinations in this series were done according to the Folin-Wu technic.

that the animals underwent dehydration, had an increase in rectal temperature of about 2.5° F., and (in spite of the glucose-loading) exhibited a fall in glucose levels from control at the end of 4 hours. The next 3 dogs were given an increased dosage, 1 percent body wt./hr. of 11 percent glucose, and tested as before. It was found (table I), that once again the animals went into dehydration and hyperthermia, and became hypoglycemic at the end of 4 hours. As the load of glucose given was sufficient to elevate the blood sugar during the first 2 hours, it was felt that by maintaining this load and, in addition, increasing the volume of fluid so as to prevent dehydration, perhaps hypoglycemia could be prevented. Accordingly 3 more dogs were given 2 percent body wt./hr. of a 5.5 percent glucose solution. It was found that dehydration was prevented in 2 of the 3 animals, but once again, blood sugar declined. The last experiment was a control run in which a dog was given the test dose of 1 percent body wt./hr. of 11 percent glucose without exposure to heat. Here the typical hyperglycemic curve was observed with glucose levels still above control values at the end of 4 hours. As shown in figure 1 the control dog had a marked diuresis while the heat-exposed animals did not. The results on the handling of glucose loads indicate that there is, indeed, an effective hypoglycemic mechanism in operation during exposure of unanesthetized dogs to heat and low humidity.

The effect of acid-base balance on glucose regulation during exposure to heat

With sufficient evidence that unanesthetized dogs exposed to heat would show a fall in

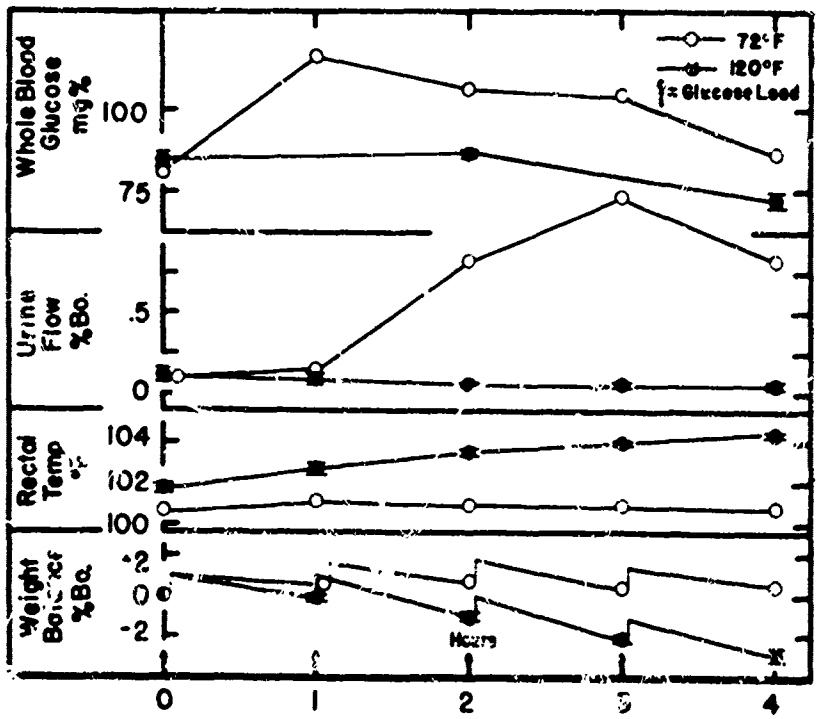


FIGURE 1

Whole blood glucose concentration, urine flow (percent body wt./hr.), rectal temperature, and weight balance (percent body weight). Closed circles – *3 dogs exposed to 120° F. air temperature.* Open circle – *1 dog exposed to 72° F. air temperature. Average standard errors of mean are included for closed-circle group. Both groups were given 1 percent body weight of an 11 percent glucose solution by stomach tube every hour for 4 hours starting just after the control period.*

blood sugar in spite of glucose-loading and independent of fluid loss, the problem of investigating the hypoglycemic mechanism itself was undertaken.

The initial study on the mechanism involved in the fall in glucose centered about the disturbance in acid-base balance that occurs in dogs exposed to heat. In attempting to regulate their deep body temperatures the animals speed up the passage of air over their oral surfaces, thereby increasing the evaporative cooling rate. This acceleration of passage of air is the panting mechanism. It has also been shown that panting is actually hyperventilation (7). Carbon dioxide is blown off, the arterial and urinary pH increases, and excess bicarbonate is excreted in the urine.

The question that immediately arose was whether the hypoglycemia was due to the respiratory alkalosis. In a series of 11 experiments the effects of both acidosis and alkalosis were investigated. Two dogs were given 12 cc./kg. of 2 percent $NaHCO_3$ by stomach tube under control conditions (no heat) to see if metabolically produced alkalosis would cause hypoglycemia. The results, table II, show that there was no significant change in whole blood glucose. Two dogs were then given a greater load of bicarbonate (20 cc./kg. of 2 percent $NaHCO_3$) under control conditions and again there was no significant change in whole blood glucose. Apparently, alkalosis, at least as produced by bicarbonate administration, does not play a role in the hypoglycemic mechanism. To be sure that we had given enough alkali to cause an alkalosis, although data in the literature showed that our previous doses were sufficient, we gave another dog a load of 20 cc./kg. of a mixture of 1 percent Na_2CO_3 and 1 percent $NaHCO_3$ while it was in the control room. Once again no significant change in whole blood glucose occurred. It can be concluded from these studies that alkalosis per se is not part of the hypoglycemic mechanism.

In 2 previously unused dogs we decided to produce a combined metabolic and respiratory alkalosis by giving the animals 20 cc./kg. of 2 percent $NaHCO_3$ and then placing them in the hot room at 124° F. The combined stress of metabolic alkalosis and heat proved to be too difficult for dog A to cope with for at the

TABLE II

Effect of metabolic alkalosis on glucose regulation

Solution	Dose (cc./kg.)	Exper. No.	Whole blood glucose — mg. percent					
			Hours					
			0	1	2	3	4	5
2 percent $NaHCO_3$	12	160	76.3	79.1	74.4	76.9	76.7	73.1
		161	69.4	71.5	68.8	69.7	68.3	68.6
2 percent $NaHCO_3$	20	162	65.0	70.9	70.9	—	66.5	—
		163	65.0	71.6	69.7	65.9	66.2	—
1 percent Na_2CO_3 and 1 percent $NaHCO_3$	20	164	75.0	73.1	72.2	72.8	—	—

Five dogs were given a dose of alkaline solution by stomach tube at the outset of the experiment. They were then tested for varying lengths of time under control environmental conditions (74° F.).

end of 3 hours the experiment was ended with the animal in obvious distress (table III). The normal defense against a metabolic alkalosis is usually excretion of bicarbonate combined with respiratory compensation in the direction of increasing the CO_2 content by depressing respiratory rate and volume of exchange. As the dog utilizes the respiratory passages as its major means of evaporative cooling, here was a situation where maintaining body temperature by panting intensified the alkalosis (increased arterial pH) by compounding the metabolic alkalosis with a respiratory alkalosis. The animal could not satisfactorily meet the situation; rectal temperature rose rapidly in spite of the panting which did occur and blood glucose fell, though not as markedly as when panting was not inhibited by a metabolic alkalosis.

While a combined respiratory and metabolic alkalosis is a serious strain on the regulatory mechanism, some animals can satisfactorily handle the load given dog A. Dog B managed to regulate its body temperature by panting sufficiently well to last through the 4 hours' exposure with only a 3° F. increase in rectal temperature (table III). Here the whole blood glucose fell gradually until the last 2 hours when the animal, having solved a large share of its metabolic alkalosis problem, presumably by renal compensation, was able to pant vigorously enough to prevent the explosive rise of rectal temperature seen in the other dog. During these last 2 hours the major fall in glucose was accomplished. Undoubtedly larger loads of alkali would be less well tolerated.

Of general interest was the effect of acidosis on blood glucose regulation. Two dogs were given 5.0 ml./kg./hr. of 1 percent HCl by stomach tube while in the hot room at 120° F. The animals encountered some difficulty in retaining all of the solution given. Whole blood glucose fell only slightly during most of the exposure but returned to just above control values at the end of 4 hours. Evidently acid per se has a hyperglycemic effect (8). There also appears to be some beneficial effect of acid-loading on temperature regulation in dogs.

Two possible mechanisms for the fall in glucose concentration during exposure to heat and dehydration remain:

1. An insulin or insulinlike action, which may take place when a dog is exposed to high environmental temperature (deposition of glucose as glycogen).

2. An increased utilization of glucose (fall in glucose due to accelerated metabolism).

Is the hypoglycemia due to an insulin or insulinlike effect?

The hypoglycemic effect of heat might be due to an insulin or insulinlike action (9,10,11) which takes place when a dog is exposed to

TABLE III

Effect of combined metabolic and respiratory alkalosis on glucose regulation

	Dog A				Dog B				
	Hours				Hours				
	0	1	2	3	0	1	2	3	4
Whole blood glucose (mg. percent)	76.0	68.4	63.1	69.1	77.2	76.5	71.3	65.6	58.4
Rectal temperature (° F.)	101.6	102.3	104.4	107.0	101.3	102.4	103.3	103.7	104.2
Weight (kg.)	16.39	16.14	15.87	15.51	17.27	17.36	17.03	16.84	16.43

Two dogs were given 50 cc./kg. of 2 percent $NaHCO_3$ by stomach tube and then placed in the hot room at 124° F.

high environmental temperatures. If so, then upon exposure to heat with no insulin available to the animal, there should be no fall in glucose concentration. This approach has been tried in 1 dog. Alloxan diabetes was produced by giving 100 mg./kg. of alloxan intravenously in a 5 percent solution, as recommended by Goldner (12). Glucose (2 percent body weight of a 5 percent solution) was given 3 hours later to prevent severe hypoglycemia due to an outpouring of remaining insulin. The next day the animal was exposed for 2 hours in the hot room at 120° F. Its ability to regulate its body temperature was seriously impaired and at the end of 2 hours rectal temperature was 106.2° F. In spite of a 3 percent body weight dehydration both whole blood and plasma glucose concentration decreased (table IV).

The pancreas was not examined histologically, but presumably the pancreatic source of insulin was destroyed, for according to the literature the dosage of alloxan that we gave was sufficient. The blood glucose levels prior to exposure to heat (table IV) were distinctly hyperglycemic. Apparently, then, the fall in glucose is not due to an insulin action, for with the pancreatic source of insulin destroyed, the tendency toward hypoglycemia still occurs upon exposure to heat and dehydration.

The effect of "lower" high environmental temperatures

One major difference in temperature regulation in man and dog is that man utilizes evaporation of sweat released from sweat glands distributed over the entire surface of the body

TABLE IV

Protocol of alloxan experiment

Date and time				
9 Apr. 1956	2:00 p. m.	Control	Whole blood glucose	77.1 mg. percent
			Plasma glucose	121.3 mg. percent
			Plasma phosphate	3.3 mg. percent P
			Weight	7.50 kg.
	2:05 p. m.	15 cc. of 5 percent alloxan solution given intravenously (dosage level, 100 mg./kg.)		
	5:00 p. m.	2 percent body weight (150 cc.) of 5 percent glucose given by stomach tube		
10 Apr. 1956	8:45 a. m.		Whole blood glucose	103.1 mg. percent
			Plasma glucose	167.5 mg. percent
			Plasma phosphate	4.2 mg. percent P
			Weight	7.30 kg.
			Rectal temperature	101.6° F.
	8:50 a. m.	Dog placed in hot room at 115° F. air temperature		
	10:50 a. m.		Whole blood glucose	90.9 mg. percent
			Plasma glucose	160.6 mg. percent
			Plasma phosphate	1.0 mg. percent P
			Weight	7.09 kg.
			Rectal temperature	106.2° F.

for evaporative cooling. We have previously shown that under high temperature conditions the panting of dogs is actually hyperventilation with ensuing respiratory alkalosis and excess excretion of bicarbonate. By lowering the air temperature used so as to get some dehydration with mild panting, but no serious involvement of the respiratory muscles, perhaps we could duplicate the results of the hyperglycemia that is reported to occur in man exposed to heat and dehydration.

We tested 4 dogs. They were exposed to an air temperature of 105° F. for 4 hours, with no water available. The severity of panting was sharply diminished from that at 120° F. The dogs were able to regulate their deep body temperature fairly closely, much as man does, so that in this case there was no increase in rectal temperature (fig. 2). This regulation of rectal temperature, however, cost about 3.4 percent of the body weight as water, but this dehydration was only 50 percent of that lost at higher temperature.

Here we see that the glucose level remained fairly constant as compared to a 22 percent fall at 120° F. We had apparently balanced the effect of dehydration (tendency toward hyperglycemia) and the effect of hyperthermia and panting (tendency toward hypoglycemia). Also the inorganic phosphate, for the first time, did not fall; at higher temperatures it always fell at least 50 percent (13).

We, therefore, did not obtain a hyperglycemia at the temperature used but, for the first time, prevented the hypoglycemia.

From this set of experiments it can be seen that with the reduction of the air temperature the hypoglycemic action is also reduced in magnitude. As at the lower levels of high environmental temperatures the need for vigorous panting is also diminished, it appears that the hypoglycemia found at high temperatures is directly related to panting. Since the respiratory alkalosis developed as a result of panting does not play a major role in the fall in blood

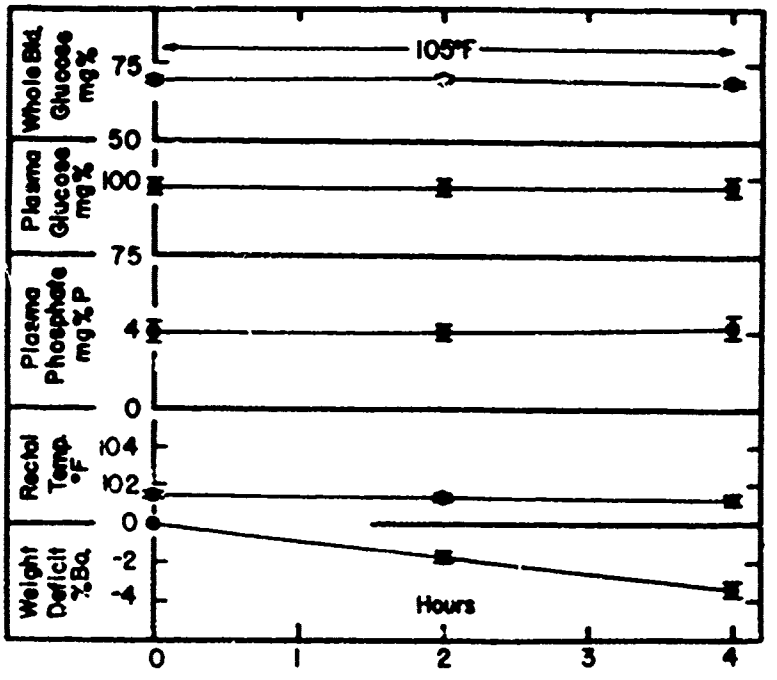


FIGURE 2

Whole blood and plasma glucose concentration, plasma phosphate concentration, rectal temperature, and weight deficit, for 4 dogs exposed to air temperature of 105° F.

glucose, one must assume that it is the exercise involving the respiratory muscles that provides the basis for the hypoglycemia. Evidently with accelerated panting glucose is utilized faster by the respiratory muscle than it can be supplied by the liver and so glucose concentration falls. Indirect proof that this is so is demonstrated above for when lower high environmental temperatures are used and panting is reduced markedly, hypoglycemia is no longer present. There is still a mild hypoglycemic action occurring but it is not sufficient to override the hemoconcentration effects of dehydration. If it were not for this hypoglycemic action, dehydration and adrenal stimulation would cause a hyperglycemia at the temperature tested.

The effects of very high temperature on glucose regulation

It was previously found that exposure to 120° F. caused hypoglycemia in dogs. Would exposure to a higher air temperature cause a greater fall in blood glucose? In order to investigate this point 2 dogs were exposed to an air temperature of 135° F. and low humidity. One dog tolerated the very high temperature for 3 hours, while the other tolerated the heat for 5 hours. When the rectal temperature reached about 106° F. the animals were removed from the hot room and the run was stopped. Here, again, hypoglycemia occurred: in one dog, 73 to 54 mg. percent, or a fall of 26 percent; in the other dog, 76 to 60 mg. percent, or a fall of 21 percent (fig. 3). Neither fall was significantly different from the results at 120° F. The striking difference was the more rapid rate of attainment of hypoglycemic levels at 135° F.

Effect of curarization on glucose regulation

All our previous work thus strongly indicated that the hypoglycemia which occurred in dogs during exposure to high environmental temperatures was due to the hyperactivity of the respiratory muscles under the aforementioned conditions. To test this hypothesis, it was reasoned that if the skeletal musculature

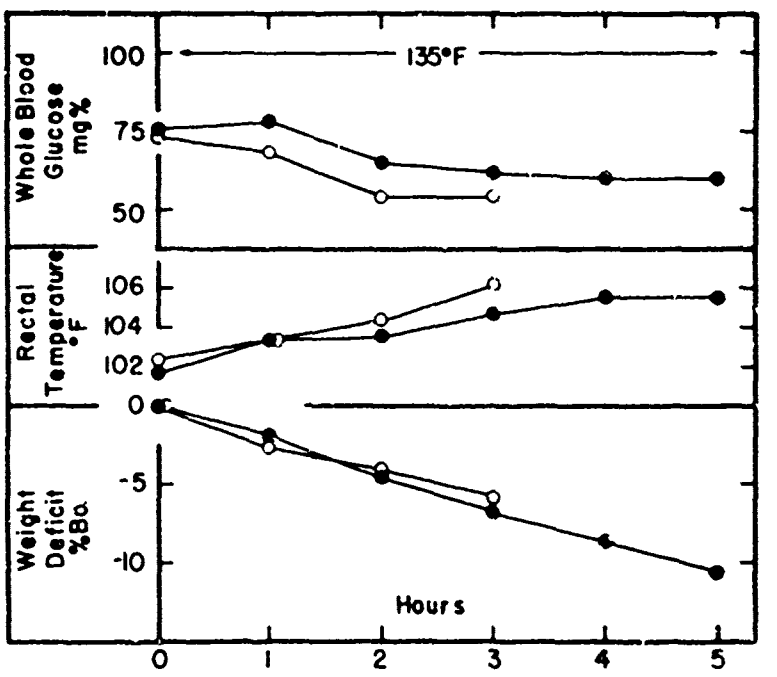


FIGURE 3

Whole blood glucose concentration, rectal temperature, and weight deficit for 2 dogs exposed to air temperature of 135° F.

were to be inactivated during exposure of dogs to heat, and if no hypoglycemia occurred (while it had occurred previously during exposure to heat without paralysis of skeletal muscle), then the previously found hypoglycemia could be attributed to the activity of the skeletal muscle. As the dogs were previously tested while standing quietly (except for panting), unrestrained in a stall, it would appear that any large increase in skeletal muscle metabolism must be largely attributed to the respiratory machine directly.

After tests were made for methodology and dosage, 2 fresh, unanesthetized dogs were exposed to heat and dehydration under the influence of flaxedil[8]. The initial dosage of flaxedil[8] was 0.07 cc./kg. This level produced muscular paralysis. The animals were placed on a dog board and artificial respiration was instituted immediately after administration of flaxedil[8] and maintained throughout the control and exposure periods. Exposure was limited to 2 hours owing to the fact that with artificial respiration, temperature regulation became more difficult and a rapid and limiting hyperthermia developed (table V).

Here we see that, as exposure to heat continued, dehydration caused a concentration of blood glucose and hyperglycemia occurred. The initial increase during the control period was largely due to excitation. The process of oral intubation for artificial respiration provided some basis for irritation and excitation and it was not surprising that sympathetic stimulation caused an initial increase in the blood glucose. It is important to note that the level of blood glucose continued to rise in the hot room and this was due mainly to dehydration. To eliminate the role of excitation in the curarization procedure another dog was tested as before, except that it was anesthetized prior to the administration of flaxedil[8]. It was found

TABLE V

Effect of curarization and hyperthermia on glucose regulation

Time	
10:00 a. m.	*Dog wt., 18.76 kg.; R. T., 103.2° F.; A. T. 78° F.*
10:15	*Blood 1* *R. T., 103.2° F., blood glucose, 67.0 mg. percent*
10:25	Gave 1.0 cc flaxedil[8] I. V. (Flaxedil[8] contained 20 mg./cc.) Dog placed on animal board and intubated. Artificial respiration instituted.
10:50	Gave 0.5 cc. flaxedil[8] I. V.
11:00	*Blood 2* *A. T., 78° F.; R. T. 103.2° F.; blood glucose, 91.4 mg. percent.*
11:02	Dog moved into hot room. A. T, 110° F.
11:05	Gave 1.0 cc. flaxedil[8] I. V.
11:45	Gave 0.5 cc. flaxedil[8] I. V.
12:00 m.	*Blood 3* *A. T., 111° F.; R. T., 105.8° F.; blood glucose, 109.0 mg. percent.*
12:10 p. m.	Gave 1.0 cc. flaxedil[8] I. V.
1:00	*Blood 4* *A. T., 115° F.; R. T., 108.4° F.; blood glucose, 107.2 mg. percent.*
1:05	Dog weighed. Wt., 17.94 kg.
1:07	Removed dog from hot room.

Protocol of experiment No. 186. R. T., rectal temperature; A. T., air temperature.

that under anesthesia the glucose level did not increase, as it did before, during the control period after giving the flaxedil®, but upon exposure of the animal to heat a steady increase in glucose concentration occurred as dehydration became progressively greater. As no fall in blood glucose occurred as it did in non-curarized, heat-exposed dogs, it appears that the hypoglycemia previously found was directly due to respiratory muscle activity. While such evidence is not direct, in conjunction with all of our previous studies, it makes such a conclusion seem more than justified.

DISCUSSION

When unanesthetized dogs are exposed to heat, hypoglycemia ensues. This finding is apparently opposite to the results obtained in man under similar environmental conditions (2, 3). The question of interest is: Are the two findings in opposition? A survey of the literature shows a somewhat confusing and incomplete picture. To resolve the problem one must view the various reports in their proper frame of reference.

Why do unanesthetized dogs show a fall in plasma glucose when exposed to high environmental temperature? One would expect that dehydration physically should cause an increase in blood glucose concentration, much as was found in man (2). The tendency is present in dogs but the utilization of glucose is sufficiently rapid to cause a fall in glucose levels. This increased utilization has been demonstrated to be due mainly to involvement of the respiratory muscles which are used in the panting mechanism. With exposure to high environmental temperature, the dog (being largely devoid of active skin sweat glands), can regulate its deep body temperature only by the evaporation of fluid from the oral surfaces (14). Speeding up the passage of air over these surfaces and in and out of the lungs by panting accelerates the evaporation of water and so cools the dog more quickly. Severe panting requires a considerable expenditure of energy, as demonstrated by the resulting hypoglycemia. The dog tolerates increasing humidity quite poorly as the panting mechanism is not too efficient even under optimal conditions. Man, on the other hand, when faced with high temperature stress manages to regulate his body temperature quite closely by profuse sweating and subsequent evaporation over the entire body surface. Ordinarily his deep body temperature does not increase more than 0.5° C., but with prolonged exercise, an elevation of deep body temperature accompanies the dehydration. Here the glucose levels vary both with the rate of work and the air temperature (15, 16). Exercise plus heat exposure has an even greater debilitating effect and the fall in glucose is more pronounced. The issue is somewhat obscured here for the fall in glucose can be ascribed to the exercise and not to the heat stress. Actually, the fall in glucose levels in dogs exposed to heat was due also to exercise — but exercise of the respiratory muscles. Can a comparable situation be found in man?

Theoretically, if under high temperature conditions one raises the humidity around the sweat glands, as with impermeable clothing, so that the sweat pours off but does not evaporate, cooling does not occur and deep body temperature increases. Under such conditions the only mechanism left is panting. In man, the physiology of hot baths demonstrates this nicely, for with an increase in deep body temperature of sufficient magnitude hyperpnea is triggered off. Haldane reported in 1905 that hyperpnea became noticeable when the rectal temperature increased above 102° F. (17). Other investigators (18, 19, 20) have reported on the increase in minute volume, the fall in CO_2 tension, and the development of alkalosis in man submerged in warm water. This, again, is the typical picture found in dogs exposed to heat. Indeed, Bazett (21), in 1927, commented expressly on the use of respiratory muscle in response to heat stress in man. The evidence shows that the hypoglycemic mechanism present in dogs is not a species phenomenon but is probably also present in man under appropriate conditions. An evaluation of temperature regulation in man and dog points to the possible interpretations.

Although dogs dissipate a larger proportion of heat from their respiratory passages than

man under high temperatures, man is superior in temperature regulation for he can more satisfactorily dissipate heat from his entire body surface. Under low humidity–high temperature conditions, body temperature in man ordinarily does not rise sufficiently for panting to occur, but along with concomitant dehydration which does occur, one usually finds an increase in blood glucose. With heat stress sufficient to raise deep body temperature to more than 102° F., sharply increased respiration occurs and a tendency toward hypoglycemia is present. Usually the respiratory involvement is not severe enough actually to overcome the effects of dehydration and so hypoglycemia does not occur. In hot baths man apparently duplicates some of the findings in dogs for here sweating is to no avail except to accelerate dehydration, which leads to concentration of blood constituents. Panting invariably results at higher core temperatures and the marked involvement of the respiratory muscles forms the same basis for hypoglycemia as in the dog.

One may, perhaps, also infer that with increased humidity (other than in baths) under high temperature conditions the respiratory muscles will also become involved in the attempt to maintain deep body temperature and prevent thermal explosion. If the humidity is sufficiently high, temperature cannot be maintained but before heat stroke occurs, the debilitating effects of reduced alveolar P_{CO_2} and perhaps hypoglycemia may become apparent. In both man and the dog the occurrence of hypoglycemia depends on the degree of involvement of the respiratory apparatus.

The technical assistance of Miss R. H. Lubinski is acknowledged.

REFERENCES

1. Kanter, G. S. Hypoglycemic effect of high environmental temperature on dogs. Am. J. Physiol. 188:443-446 (1957).
2. Adolph, E. F. Physiology of man in the desert. New York: Interscience Publishers, Inc., 1947.
3. Pitts, G. C., R. E. Johnson, and F. C. Consolazio. Work in the heat as affected by intake of water, salt and glucose. Am. J. Physiol. 142:253-259 (1944).
4. Nelson, N. A photometric adaptation of the Somogyi method for the determination of glucose. J. Biol. Chem. 153:375-380 (1944).
5. Somogyi, M. Notes on sugar determination. J. Biol. Chem. 195:19-23 (1952).
6. Gomori, G. A modification of the colorimetric phosphorous determination for use with the photoelectric colorimeter. J. Lab. Clin. Med. 27:955-960 (1941).
7. Kanter, G. S. Effect of heat on regulation of body fluids and electrolytes in dogs. Am. J. Physiol. 178:259-262 (1954).
8. Elias, H. Ueber die Rolle der Saure im Kohlenhydratatoffwechsel ueber Saurediabetes. Biochem. ztschr. 48:120-143 (1913).
9. Britton, S. W. Studies on the conditions of activity in endocrine glands. Am. J. Physiol. 74:291-308 (1925).
10. Clark, G. A. The influence of the vagus on the islets of Langerhans. III. The effect of cutting the vagus upon sugar tolerance. J. Physiol. 61:576-582 (1926).
11. Rodbard, S., and M. S. Goldstein. Neurogenic control of the blood sugar elicited by induced variations in the body temperature of the chick. Am. J. Physiol. 162:175-181 (1950).
12. Goldner, M. G. Alloxan diabetes its production and mechanism. Bull. New York Acad. Med. 21:44-55 (1945).
13. Kanter, G. S., and R. H. Lubinski. Effect of heat on inorganic phosphate regulation in dogs. Am. J. Physiol. 180:559-562 (1955).
14. Dill, D. B., A. V. Bock, and H. T. Edwards. Mechanisms for dissipating heat in man and dog. Am. J. Physiol. 104:36-43 (1933).
15. Levine, S. A., B. Gordon, and C. L. Derick. Some changes in the chemical constituents of the blood following a marathon race. J.A.M.A. 82:1778-1779 (1924).

16. Gordon, B., L. A. Kohn, S. A. Levine, M. Matton, W. M. Scriver, and W. B. Whiting. Sugar content of the blood in runners following a marathon race. J.A.M.A. 85:508-509 (1925).

17. Haldane, J. S. The influence of high air temperatures. J. Hyg. 5:494-513 (1905).

18. Hill, L., and M. Flack. The influence of hot baths on pulse frequency, blood pressure, body temperature, breathing volume and alveolar tension of man. J. Physiol. 38:57-61 (1909).

19. Bazett, H. C., and J. B. S. Haldane. Some effects of hot baths on man. J. Physiol. 55:iv-v (1921).

20. Koehler, A. E. Acid-base equilibrium. I. Clinical studies in alkalosis. Arch. Int. Med. 31:590-605 (1923).

21. Bazett, H. C. Physiological responses to heat. Physiol. Rev. 7:531-599 (1927).